Additional Presentation Abstracts

Monday, June 12, 2006

Workshop 6
Negative Symptoms of Schizophrenia: Methodological Hurdles to Achieving an Indication
2:45 p.m.–4:15 p.m.

NIMH Perspective on Assessment of Negative Symptoms

Wayne S. Fenton, M.D.
National Institute of Mental Health

Supporting activities to hasten the development of new therapeutics for mental illness is a major priority of the NIMH Division of Adult Translational Research and Treatment Development. As described in the FDA Report: *Innovation or Stagnation? Challenge and Opportunity on the Critical Path to New Medical Products*, creating new or more sensitive endpoints for use in clinical trials can enhance the efficiency of therapeutics development. Consequently, developing, testing, and validating methods to assess domains of psychopathology for use in clinical trials is an additional NIMH priority. Because negative symptoms represent a major unmet therapeutic need in schizophrenia, NIMH has supported a process to re-evaluate current approaches to assessment of these symptoms with the possibility of developing a more sensitive second-generation assessment tool.

Learning objectives:
- To understand the prognostic significance of negative symptoms in schizophrenia.
- To understand limitations of existing negative symptom assessment tools.
- To better understand NIMH priorities for treatment development.

Tuesday, June 13, 2006

Plenary Session
The Value and Limitations of Large Practical Clinical Trials in Informing Practice
8:45 a.m.–12:00 p.m.

The Public Mental Health Perspective

Renata J. Henry, M.Ed.
Delaware Department of Health and Social Services, Division of Substance Abuse and Mental Health

The results of the near completed large clinical trials offer a wealth of scientific knowledge to the public mental health field, with more information yet to come. The good news is that mental health consumers, clinicians, and administrators will be able to make better informed decisions about quality care and mental health policy. The challenge of moving the science into service will be discussed. Dissemination of the information, adoption of new information, making change in policy and practice, and identifying the new research questions are the topics that will be explored.

Learning Objectives:
- Participants will understand the challenges associated with dissemination of information in the public mental health system.
- Participants will understand the challenges associated with moving science to service.
- Participants will learn about the partnerships required to move science to service.

Panel 3
STAR*D – What Have We Learned?
2:00 p.m.–5:00 p.m.

STAR*D Level 2 Medication Treatment

A. John Rush, M.D.
University of Texas Southwestern Medical Center

Overall, 1439 patients enrolled in the second treatment step (Level 2) in STAR*D. Only 21 patients found all seven treatment options acceptable (e.g., allowed themselves to be randomized to all seven options). Roughly half accepted either a switch to another treatment, which included 3 acute depressant medications or cognitive therapy. Conversely, about half accepted randomization to one of two augmentation medications (buspirone or bupropion-SR) or augmentation with cognitive therapy. This presentation will summarize the acute outcomes with the 3 switch medications (bupropion-SR, sertraline, venlafaxin-SR) and with the two augmentation medications. By and large, these comparisons revealed very similar remission rates, time to remission and response, and time to response rates. Some secondary measures did favor bupropion as medication augmentation. The implications for practice will be discussed. Selective aspects of the longer-term naturalistic follow-up will be presented.

Learning Objectives:
- The participant will be able to determine whether pharmacological differences in second step medication treatments are associated with different degrees of symptom improvement or tolerability.
- The participant will be able to determine whether the pharmacological differences in augmentation medications are associated with different degrees of symptom reduction or tolerability in the second treatment step.

Panel 3
STAR*D – What Have We Learned?
2:00 p.m.–5:00 p.m.

STAR*D Level 3 Acute and Longer-Term Outcomes

Andrew A. Nierenberg, M.D.
Massachusetts General Hospital

Over 370 patients enrolled in STAR*D Level 3. All of these patients had not had an adequate benefit with at least two prior medication treatments. For a small subset of these patients, cognitive therapy had also failed to achieve remission. As in the second treatment step (Level 2), most patients preferred either to receive one of two switch treatments (mirtazapine or nortriptyline, randomized) or one of two augmentation treatments (lithium or T3, randomized). This presentation will describe the sample that received each of these strategies (augment or switch) and it will report on the symptomatic outcomes with the secondary measure (the Quick Inventory of Depressive Symptoms – Self-Report) (QIDS-SR) and on the relative tolerability and safety of each treatment. Overall, longer-term outcomes of medication switching and medication augmentation at this third medication treatment step will be discussed.

Learning Objectives:
- Be able to determine whether different pharmacological mechanisms result in differential symptom benefit or tolerability at the third medication treatment step (either augmentation or switch).
- Be able to describe the longer-term outcomes of patients who respond or remit with medication at the third medication treatment step.

Tuesday, June 13, 2006 continued

Panel 4
Translational Research in Geriatric Psychiatry: Implications for Symptomatic and Preventative Interventions

Clinical Development Issues for Geriatric Psychiatry

Herbert W. Harris, M.D., Ph.D.
Jazz Pharmaceuticals

This presentation will focus on clinical trial issues associated with mental disorders of late life. Depression will be used as a paradigm for the exploration of efficacy and tolerability issues that are uniquely relevant to the elderly. With regard to efficacy, the paradigms of acute symptomatic treatment, disease modification, and relapse prevention will be discussed. Traditionally, most clinical antidepressant trials have focused on acute efficacy as the primary outcome. However, a review of the natural history and underlying biology of late life depression suggests that relapse prevention and disease modification are potentially important approaches to treatment. With regard to tolerability, the elderly are often noted to be more sensitive to various side effects associated with antidepressants. To the extent that these side effects are correlated with the therapeutic mechanism of action, issues associated with tolerability will have major impact on the detection of efficacy signals in this population.

Learning Objectives:
- Participants will understand differences between disease modification strategies, relapse prevention, and symptomatic treatments in clinical drug development.
- Participants will understand how concepts of disease modification and relapse prevention may be applied to late life depression and other disorders of late life.
- Participants will gain greater appreciation of the interactions between efficacy and tolerability in geriatric clinical trials.
- Participants should be able to contrast the role of tolerability in trials involving elderly and young adult populations.

Thursday, June 15, 2006

Food and Drug Administration Symposium
9:00 a.m.–12:00 p.m.

Managing Risk During Drug Development

Paul J. Andreason, M.D.
Acting Deputy Director, Division of Psychiatry Products

Every new drug will likely have some use-related problems that were not observed in its initial development program. This is inevitable and this very inevitability is too frequently ignored by the public and press. Fifteen years ago, the US was one of the last major countries in the world to make a new drug available. Though US citizens were not able to benefit from the positive aspects of newer drugs sooner than other countries, they were protected from these problems that appeared in the countries where the drug was initially approved. In August of 1962 the FDA reviewer Frances O. Kelsey found problems with thalidomide in the offspring of non-US patients. She was given the President's Award for Distinguished Federal Civilian Service by President John Kennedy. She was cited for resisting the sale of thalidomide in the United States, thereby preventing the birth of thousands of deformed babies in the United States as happened in Germany, Great Britain, Canada, and numerous other countries in the late 1950s and early '60s. During the AIDS crisis, the Agency was told that the US was unacceptably slow at getting drugs to market. The Prescription Drug User Fee Act provided the mechanism for drugs to be reviewed and approved faster. This, in turn, leads to the US more often being among the first countries to approve new drugs. The downside of being the first country where a new drug is approved is that its citizens are the population at risk for rare and yet unknown drug-related serious adverse events. This will be true for whatever country is the first to approve a new drug. It is also true that the last country to approve a drug will have the benefit of everyone else's experience and the last to reap any potential benefit.

Learning Objectives:
- What are the ICH guidelines for patient exposure for drugs used for chronic and non-life-threatening conditions?
- What is the "rule-of-three" and how does this relate to known risk at the time of drug approval using the ICH guidelines?
- Give an example of a rare and serious adverse event that was not discovered until after initial drug approval.